Yale Primary Care Residency Program

Hepatitis Clinic Primer

2018-2019
4th Edition

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Introduction to Hepatitis Clinic at SRC-APC

Welcome to the hepatitis clinic!

The goal of this primer is to provide a resource to residents in navigating various topics in hepatitis management. Our hope is that the primer in conjunction with clinic experience will allow residents to feel more comfortable and confident in evaluating and treating patients with hepatitis B and C.

Hepatitis clinic Inclusion Criteria

- Mono-infected hepatitis C (HCV) patients (No HIV)
- Mono-infected hepatitis B (HBV) patients
- Co-infected HBV and HCV patients
- Exclude decompensated cirrhosis

Services Provided by the Clinic

- Initial consultation
- Assessment for possible initiation of anti-viral therapy
- Follow treatment course for patients on anti-viral treatment

Hepatitis Clinic Attendings

Dr. Andre Sofair went to medical school at the Albert Einstein College of Medicine and was a resident and chief resident at Yale. After practicing medicine in rural New Hampshire for four years, he returned to join the faculty of the Yale Primary Care Program where he works both in the inpatient and outpatient setting and serves as one of the inpatient Firm Chiefs. His research interests include the epidemiology of infectious diseases, viral hepatitis, and post-graduate educational systems.

Dr. Joe Canterino completed his residency training and chief residency in the traditional internal medicine program at Yale-New Haven Hospital. He then completed Infectious Diseases fellowship at Yale as well, where he spent his last year of training treating hepatitis C at the West Haven VA hospital. He is now on the ID faculty at Yale, primarily based at the St. Raphael's campus.

Facts about Hepatitis C

- The hepatitis C virus infects hepatocytes, replicates within the cytoplasm, and is then secreted from the cell.

- According to the CDC, approximately 3.5 million persons in the United States have chronic HCV infection.

- There are at least 6 major genotypes of HCV with many subtypes[1]:

  Genotype 1
  - Most common genotype in the United States and worldwide.
  - About 70-80% of cases in the U.S.

  Genotype 2
  - Second most common genotype in the United States and worldwide.
  - About 10-20% of cases.

  Genotype 3
  - Mostly endemic in Southeast Asia. Also found in India and Australia.

  Genotype 4
  - Most common in Africa (Egypt) and Middle East.

  Genotype 5
  - Most common in South Africa.

  Genotype 6
  - Most common in Southeast Asian countries.

- Most patients who are infected with HCV do not spontaneously clear the virus. Approximately 75 to 85% of patients develop chronic HCV infection, which may result in liver fibrosis and cirrhosis.

- Per CDC, of every 100 persons infected with HCV, approximately
  - 75-85 will develop chronic infection
  - 60-70 will develop chronic liver disease
  - 15-20 will develop cirrhosis over a period of 20-30 years
  - 1-5 will die from sequelae of chronic infection (liver cancer or cirrhosis)

- Conditions associated with hepatitis C infection include: mixed cryoglobulinemia, porphyria cutanea tarda, lichen planus, necrolytic acral erythema, thrombocytopenia, glomerulonephritis, diabetes mellitus, autoimmune thyroiditis, and B-cell lymphoproliferative disorders[2].

- Individuals with HCV can often be co-infected with HIV due to the prevalence of IV drug use. According to the CDC, in individuals who acquired HIV through IV drug use, about 50-90% are co-infected with HCV. When all methods of transmission of HIV are considered, on average 25% of individuals with HIV are co-infected with HCV.

Whom to Screen for Hepatitis C?

Screening is important as patients with hepatitis C are frequently asymptomatic, and many individuals do not know they have chronic HCV infection.

According to CDC and AASLD recommendations, physicians should only screen patients who have prior or ongoing risk factors for HCV exposure, including[3]:

- patients born in 1945 through 1965, regardless of country of origin
- history of illicit IV drug use or intranasal cocaine use (even one time use)
- HIV infection
- history of incarceration
- transfusion of clotting factors made before 1987
- transfusion of blood/transplant of organs before July 1992
- chronic hemodialysis
- tattoos from unregulated settings
- evidence of liver disease (persistently elevated alanine aminotransferase level)
- needle stick injury or mucosal exposure to HCV-positive blood
- patients who have been informed that they received blood from a donor who later tested positive for HCV
- presence of extrahepatic manifestations associated with HCV, such as mixed cryoglobulinemia or porphyria cutanea tarda
- while not included in AASLD recommendations, consider screening patients with current sexual partners who are HCV-infected

Hepatitis C Screening and Serology

1) Obtain hepatitis C antibody → If (-), generally indicates absence of chronic hepatitis C infection.

   Exceptions include:

   - Immunocompromised patients (eg, HIV infected patients, transplant recipients, or patients on hemodialysis) may not have detectable levels of antibodies despite having HCV infection. In this case, further testing for HCV RNA may be prudent to exclude infection.

   - Acutely infected patients may require additional HCV RNA testing given that antibodies may take months to develop.

2) If hepatitis C antibody (+) or indeterminate, obtain HCV quantitative RNA → If RNA is detectable, then HCV infection confirmed.

3) If HCV antibody (+) but RNA (-), the reactive antibody likely represents either a past HCV infection that was cleared (typically associated with high antibody titres) or a false positive antibody test (typically associated with low antibody titres).

4) If both HCV RNA(-) and antibody (-), this essentially confirms the absence of HCV infection.

Initial Work-Up in HCV (+) Patients

In a patient with newly diagnosed HCV, it is important to collect data that will help assess and evaluate the extent of liver damage and determine eligibility for treatment. Specifically, assessment of the appropriateness of therapy involves work-up for factors that may influence treatment response or comorbidities that would be contraindications for initiating therapy. Most patients should have these labs drawn prior to referral to hepatitis clinic.

1) Laboratory Work-Up

- HCV genotype and viral load
- Hepatitis A IgG antibody
- Hepatitis B surface antigen, surface antibody, core IgG antibody
- 4^{th} generation HIV test (Ag/Ab)
- CBC
- CMP (LFTs, bilirubin, albumin)
- INR
- Fibrosure testing (serologic testing to assess degree of hepatic inflammation and fibrosis, see page 8)
- Urinalysis (hepatitis C association with renal disease)
- Pregnancy testing (especially if possible treatment regimen to include ribavirin)

2) Radiologic Imaging

- Liver ultrasound
- FibroScan (transient elastography)
- Liver biopsy if needed

Initial Hepatitis C Clinic Visit

1) Obtain further history:
   - Attempt to identify source of infection.
   - Assess symptoms (anorexia, weight loss, myalgias). Many patients with HCV have significant fatigue.
   - Ask about any prior exposure to HCV treatment and response.
   - Screen for past history that could suggest underlying cirrhosis: jaundice, hematemesis/GI bleeding, ascites, or encephalopathy.
   - Factors that may affect candidacy for treatment, including active substance use and medication / appointment adherence.
   - Obtain an up-to-date list of medications and vaccinations.

2) Through physical exam, laboratory, and radiologic findings, assess liver function and degree of liver fibrosis as it can affect urgency and candidacy for treatment regimens.

   Liver biopsy is the gold standard to determining degree of liver fibrosis in a patient with HCV. METAVIR staging is a commonly used system to quantify the degree of liver fibrosis seen on biopsy[4]. The METAVIR stages are scored from 0-4 (figure 1).

   However, given the invasive nature of liver biopsies, indirect means of assessing the degree of fibrosis are typically used first. These are noted on the following page.

Figure 1. METAVIR Fibrosis Staging

F0: no fibrosis
F1: minimal fibrosis
F2: fibrosis has occurred and extends outside the areas in the liver that contain blood vessels
F3: bridging fibrosis is spreading and connecting to other areas that contain fibrosis
F4: cirrhosis or advanced liver fibrosis

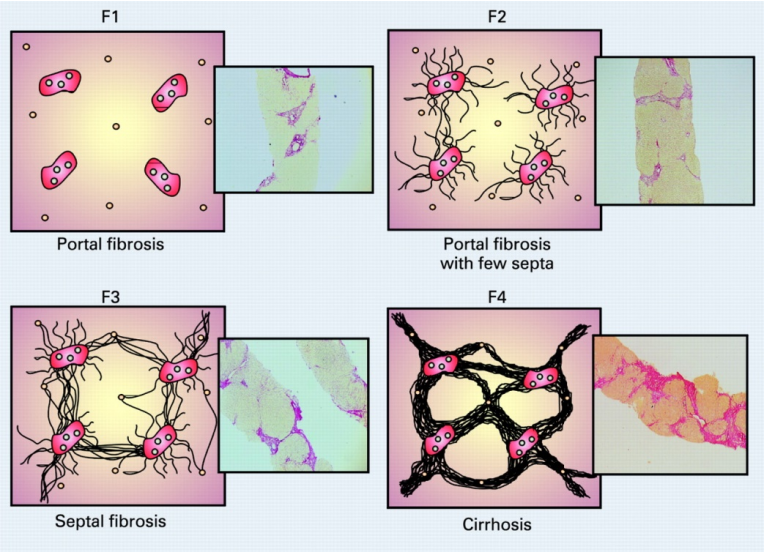

Image courtesy of http://www.pathologyoutlines.com/topic/liverchronichepgrading.html

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(Initial Hepatitis C Clinic Visit, assessment of liver function and fibrosis continued)

Physical exam findings

- A directed physical examination should assess for signs consistent with cirrhosis (end-stage fibrosis). These include jaundice, palmar erythema, spider angiomata, gynecomastia, caput medusa, firm liver on palpation, splenomegaly, shifting dullness or fluid wave, and hypogonadism[5].

Laboratory abnormalities

- Leukopenia, thrombocytopenia, hypoalbuminemia, transaminitis, hyperbilirubinemia and coagulopathy may indicate presence of advanced fibrosis and/or cirrhosis[2]. Multiple scoring algorithms to predict cirrhosis have been developed utilizing some of these laboratory tests.

- **FibroSure testing**: This is the preferred biochemical marker testing for cirrhosis in our clinic. This test is ordered through EPIC as "Fibrosure." The score is calculated by our laboratory using patient's gender, age, and the results of six serum tests: alpha-2-macroglobulin, haptoglobin, apolipoprotein A1, GGT, total bilirubin, and ALT. FibroSure scores are validated to detect cirrhosis in patients with HCV, HBV, alcoholic liver disease, and NAFLD. A FibroSure score of 0.75 or higher correlates with findings of Metavir F4 disease on liver biopsy, with a sensitivity of 56%, specificity of 81%, with positive LR of 2.9 and negative LR of 0.54[6].

- **APRI score** (AST:Platelet Ratio Index): Calculated using the formula [(Patient AST/upper limit of normal)/Platelet Count] x 100. A cutoff score of <0.7 suggests minimal fibrosis (<F2 by METAVIR); a score of >1.0 has a sensitivity of 76% and specificity of 72% for detecting severe fibrosis/cirrhosis (F3-F4)[7]. The APRI score is limited in its ability to accurately detect intermediate fibrosis, so it usually requires further clinical correlation.

- **FIB-4 score**: Calculated using the formula (Patient age x AST)/(Platelet count x $\sqrt{ALT}$). A score of >3.25 has a 98% specificity and PPV of 65% for cirrhosis; a score of <1.45 has a NPV of 90% for advanced cirrhosis[8]. Values between 1.45 and 3.25 are difficult to interpret and require additional clinical correlation.

(continued)

(Initial Hepatitis C Clinic Visit, assessment of liver function and fibrosis continued)

Imaging

- Liver ultrasound: Ultrasound of the liver can detect anatomic changes that may confirm the presence of overt cirrhosis or portal hypertension if physical exam and laboratory markers are indeterminate. Ultrasound can visualize liver nodularity, parenchymal heterogeneity, presence of perihepatic lymphadenopathy and/or splenomegaly, alterations in venous and/or arterial flow (when ordered with Doppler), and presence of hepatocellular carcinoma (HCC).

- FibroScan (liver transient elastography): FibroScan is a non-invasive test that uses ultrasound to measure liver stiffness. FibroScan results are measured from 0 to 75kPa, with a score of >15kPA indicating a >90% chance of having cirrhosis (F4 disease), and a score of >7 indicating an 85% probability of at least F1-F2 fibrosis[9]. Test results are limited by ascites and obesity.

3) Update Health Maintenance
   - Hepatitis A vaccination if seronegative
   - Hepatitis B vaccination if seronegative
   - Pneumonia vaccination if patient has cirrhosis or meets other indications
   - Inactivated Influenza vaccination yearly
   - EGD for variceal screening if patient has evidence of cirrhosis
   - Liver ultrasound for HCC screening if patient has F3 or F4 fibrosis

4) Patient education
   - Abstinence from alcohol: concurrent use with HCV infection can increase rate of hepatic fibrosis. Alcohol may also affect hepatic metabolism of anti-HCV medication.
   - Abstinence of illicit substances: concurrent use -- particularly IV and intranasal substances -- can place patients at continued risk of re-infection and also increase risk of disease transmission to others.
   - Prevention of disease transmission - patients with untreated HCV should be counseled to:
     - Avoid sharing dental and shaving equipment
     - Dispose of sharps safely and avoid use of shared syringes, needles, water, and other preparation equipment if cessation of illicit substances is unlikely
     - Avoid donation of blood.

Initiation of Hepatitis C Treatment

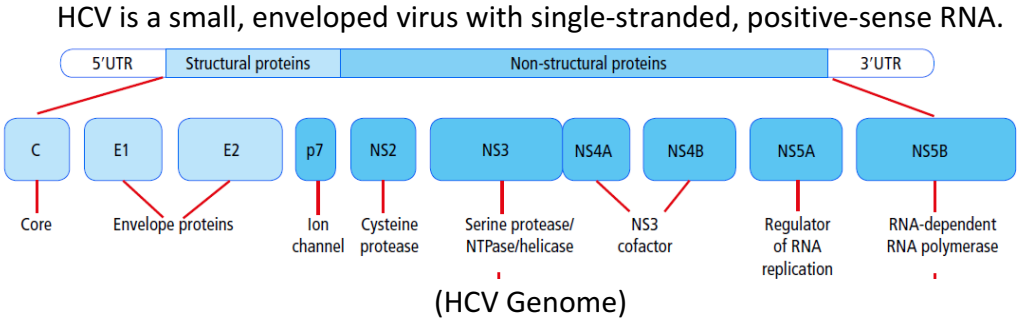
All patients with chronic HCV infection (ie, detectable HCV viral load > 6 months) should be considered for treatment.

The goal of treatment is to achieve **Sustained Virologic Response (SVR),** which is defined as absence of virus in the blood 12 weeks after the completion of treatment. Patients who have achieved SVR are for all intents and purposes considered successfully cured of HCV. These patients have improved outcomes in terms of all-cause and liver-related mortality, need for liver transplantation, and development of HCC (in non-cirrhotics).[10,11]

Up until 2011, treatment for HCV was primarily limited to pegylated-interferon (IFN) and ribavirin (RBV), with therapy often limited by long duration (at least one year), adverse side effects, and poor cure rates (~50%). Starting in 2011, the FDA began approval of oral **direct-acting antiviral (DAA)** therapies, which have largely replaced IFN and RBV therapy. Targets of current DAA therapies are shown in figure 2.

Current treatment regimens are largely determined by HCV genotype and may be further refined based on patient comorbidities and potential drug-drug interactions. Medications and regimens on the following pages are based upon AASLD/IDSA guidance as of July 2018, found at http://hcvguidelines.org/. Refer to http:hep-drugintreactions.org for a full list of drug interactions.

Figure 2. Targets of HCV Antiviral Therapy



NS5B – Function in replicating viral RNA by serving as RNA-dependent RNA polymerase.

NS5A – Zinc-binding phosphoprotein that serves as a modulator in HCV RNA replication, including regulation of NS5B.

Protease (ex, NS3, NS4) – Enzymes used for proteolysis in the assembly process of mature viral particles.

Brand Name	Generic Name	Mechanism of Action	Geno -type	Dosing	Cost*	Contraindications	Side effects	Notes
Epclusa	Sofosbuvir / Velpatasvir	NS5B/NS5A inhibitor	All	Daily	$24,754	None	Headache, fatigue, nausea, LFT abnormalities	
Mavyret	Glecaprevir + Pibrentasvir	NS3/4A, NS5A inhibitor	All	3 tabs daily	$16,615	Latent hepatitis B (cases of hep B reactivation)	Headache, nausea, diarrhea, fatigue	
Harvoni	Sofosbuvir / Ledipasvir	NS5B/NS5A polymerase inhibitor	1, 4, 5,6	Daily	$31,288	None	Fatigue, headache nausea	Avoid amiodarone, antiepileptics, rifampin, rosuvastatin
Zepatier	Elbasvir / Grazoprevir	NS5A, NS3/4A inhibitor	1,4	Daily	$18,081	Child B/C cirrhosis, caution in elderly and Asian patients	Headache, fatigue, nausea, LFT abnormalities	NS5A resistance testing needed for HCV genotype 1a
Viekira Pak	Ombitasvir/ Paritaprevir/ Ritonavir + Dasabuvir	NS5A, NS3/4A inhibitors, + NS5B inhibitor	1,4	Daily + BID Dasabuvir	$27,587	Child B/C cirrhosis	Fatigue, nausea, pruritis, rash, insomnia	Avoid salmeterol and statin use
Olysio	Simeprevir	NS3/4 inhibitor	1	Daily	$21,973	Child B/C cirrhosis, Q80K mutation(+)	Fatigue, nausea, pruritis, rash, photosensitive	Used in combination with sofosbuvir
Sovaldi	Sofosbuvir	NS5B inhibitor	All	Daily	$27,812	None	Fatigue, headache, nausea	Used in combination with other agent
Daklinza	Daclatasvir	NS5A inhibitor	1,2,3	Daily	$22,350	None	Headache, fatigue, nausea, lipase elevation	Used in combination with sofosbuvir

*Costs estimated using GoodRx for 28-day supply in New Haven, CT, as of July 2018
** Please refer to http:hep-drugintreactions.org for a full list of drug interactions

Brand Name	Generic Name	Mechanism of Action	Geno -type	Dosing	Cost*	Contraindications	Side effects	Notes
Copegus, Moderiba, Rebetol, Ribasphere	Ribavirin	Unclear	All	Daily	$150	Hg <8.5, pregnancy	Anemia, rash, cough	Typically used in 2nd line regimens for treatment-naïve patients with cirrhosis
PegIntron, Pegasys	Pegylated Interferon alpha	Antiviral immunity activator	N/A	Weekly injection	$3,600	Thrombocyto-penia, advanced cirrhosis, mental health	Bone marrow suppression, fatigue, nausea, thyroid dysfunction	No longer indicated in treatment of hepatitis C

*Costs estimated using GoodRx for 28-day supply in New Haven, CT, as of July 2018
** Please refer to http:hep-drugintreactions.org for a full list of drug interactions

AASLD/IDSA 2018 Guidance Recommended Treatment Regimens by Genotype for Treatment-Naïve Patients without Hepatic Decompensation

Genotype 1a (gray background = alternate treatments)

Regimen	Duration (weeks)	SVR12	Trials	Rating
Glecaprevir + Pibrentasvir	8 (non-cirrhosis) 12 (cirrhosis)	99%	ENDURANCE-1 EXPEDITION-1	IA IA
Elbasvir + Grazoprevir* + RBV (If NS5A RAV)	12 (all) 16 (NS5A RAV)	92-97%	C-EDGE	IA IIB
Sofosbuvir + Ledipasvir	12 (all) 8 (non-black, non HIV, HCV RNA <6mill)	93-99%	ION-1, ION3	IA IB
Sofosbuvir + Velpatasvir	12 (all)	98-99%	ASTRAL-1	IA
Sofosbuvir + Simeprevir**	12 (non-cirrhosis) 24 (cirrhosis)	88-92%	OPTIMIST-1 OPTIMIST -2	IA
Viekira Pak + RBV	12 (non-cirrhosis) 24 (cirrhosis, 2nd line)	95-97%	SAPPHIRE-I, PEARL-IV TURQUOISE-II	IA
Sofosbuvir + Daclatasvir +/- RBV	12 (non-cirrhosis) 24 (cirrhosis)	96%	ALLY-2	IB

***** About 10-15% of patients with HCV genotype 1a infections without prior treatment with NS5A inhibitors have detectable HCV NS5A resistance-associated variants which causes a >5 fold reduction in activity of NS5A inhibitors. Testing may be recommended when considering regimens containing elbasvir

****** About 30% of patients with genotype 1a have a Q80K polymorphism that causes resistance to Sofosbuvir-Simeprevir (Olysio). Olysio is not recommended for patients with cirrhosis and who are also positive for the Q80K mutation.

Genotype 1b (gray background = alternate treatments)

Regimen	Duration (weeks)	SVR12	Trials	Rating[ǂ]
Glecaprevir + Pibrentasvir	8 (non-cirrhosis) 12 (cirrhosis)	99%	ENDURANCE-1 EXPEDITION-1	IA IA
Elbasvir + Grazoprevir	12 (all)	92-97%	C-EDGE	IA
Sofosbuvir + Ledipasvir	12 (all) 8 (non-black, non HIV, HCV RNA <6mill)	93-99%	ION-1, ION3	IA IB
Sofosbuvir + Velpatasvir	12 (all)	98-99%	ASTRAL-1	IA
Sofosbuvir + Simeprevir	12 (non-cirrhosis)	88-92%	OPTIMIST-1	IA
Viekira Pak + RBV	12 (all)	95-97%	SAPPHIRE-I, PEARL-IV TURQUOISE-II	IA
Sofosbuvir + Daclatasvir	12 (non cirrhotic)	96%	ALLY-2	IB

Genotype 2 (gray background = alternate treatments)

Regimen	Duration (wks)	SVR12	Trials	Rating
Glecaprevir + Pibrentasvir	8 (non-cirrhosis) 12 (cirrhosis)	99% 99%	SURVEYOR-II EXPEDITION-1	IA IB
Sofosbuvir + Velpatasvir	12 (all, 1st line)	99-100%	ASTRAL-1 + 2	IA
Sofosbuvir + Daclatasvir	12 (non-cirrhosis) 16-24 (cirrhosis)		Wyles, 2015	IIB

Genotype 3

Regimen	Duration (wks)	SVR12	Trials	Rating
Glecaprevir + Pibrentasvir	8 (non-cirrhosis) 12 (cirrhosis)	93% 100%	ENDURANCE-3 SURVEYOR-II	IA
Sofosbuvir + Velpatasvir*	12 (all) 12 (cirrhosis)	93%	ASTRAL-3	IA
Sofosbuvir + Daclatasvir +/- RBV cirrhosis	12 (non-cirrhosis) 24 (cirrhosis)	90-93% 86%	ALLY-3 ALLY-3	IA IIB

* RAS testing for Y93H is recommended for cirrhotic patients. If present, ribavirin should be included in the regimen or sofosbuvir/velpatasvir/voxilaprevir should be considered

Genotype 4

Regimen	Duration (wks)	SVR12	Trials	Rating
Glecaprevir + Pibrentasvir	8 (non-cirrhosis) 12 (cirrhosis)	99% 100%	ENDURANCE-4 EXPEDITION-1	IA IB
Sofosbuvir + Velpatasvir	12 (all)	100%	ASTRAL-1	IA
Elbasvir + Grazoprevir	12 (all)	97-100%	C-EDGE	IIB
Sofosbuvir + Ledipasvir	12 (all)	95%	SYNERGY	IIB
Viekirax + RBV	12 (all)	100%	PEARL-I	IA

Genotype 5 & 6

Regimen	Duration (wks)	SVR12	Trials	Rating
Glecaprevir + Pibrentasvir	8 (non-cirrhosis) 12 (cirrhosis)	100% 100%	ENDURANCE-4 EXPEDITION-1	IA IA
Sofosbuvir + Velpatasvir	12 (all)	100%	ASTRAL-1	IB
Sofosbuvir + Ledipasvir	12 (all)	95%	SYNERGY	IIB

Follow-up and Monitoring

During treatment

The goals of follow-up after initiation of therapy are to assess 1) medication compliance, 2) adverse effects of therapy, 3) new drug-drug interactions, and 4) efficacy and safety of treatment.

To ensure safety and efficacy of treatment, AASLD and ISDA recommend:

- Four weeks after starting treatment, patients should have blood drawn to check CBC, creatinine, and LFTs.
- HCV quantitative RNA should be checked 4 weeks and 12 weeks post-initiation / at completion of therapy (this may be at 8 weeks of glecaprevir + pibrentasivr are used in non-cirrhotic patients). Patients with detectable RNA levels at week 4 should have repeat testing at week 6.
- Patients treated with ribavirin should have close monitoring of CBC. Females of child-bearing age should be counseled against pregnancy up to 6 months post-RBV treatment.

The AASLD and IDSA recommend cessation of therapy if patients exhibit any of the following:

- Increase in ALT activity by 10-fold within 4 weeks of treatment initiation.
- Any increase in ALT within 4 weeks of treatment initiation associated with weakness, nausea, vomiting, jaundice or an increase in bilirubin, alkaline phosphatase, or INR.
- Treatment intolerance due to other adverse side effects or safety concerns.
- HCV viral load increase by more than 10-fold on or after week 6 compared to week 4.

Post-treatment

Patients who have completed their treatment course are recommended to have quantitative HCV RNA testing at completion of treatment and at 12 weeks after treatment. Those with undetectable viral loads 12 or more weeks post-treatment have achieved SVR. We typically also check a viral load 12 months after cessation of therapy.

Patients who have achieved SVR should be assessed periodically for risk factors for reinfection or evidence of disease recurrence.

Patients who still have detectable viral loads at completion of therapy, or are unable to maintain undetectable viral loads within 12 weeks post-therapy are considered to have treatment failure or relapse, respectively. These patients need to be considered for additional treatment options. They should also receive screening for progression of liver disease with CBC, LFT, and INR q6-12 months.

(continued)

(Follow-up and monitoring, continued)

All patients regardless of SVR status post-treatment should have screening for esophageal varices if they have cirrhosis.

In 2015 the AASLD also released a recommendation based upon consensus opinion that all patients with HCV regardless of SVR status should receive HCC screening with liver ultrasound q6 months if they have stage F3 or F4 fibrosis. The inclusion of stage F3 patients remains somewhat controversial within the GI community, but was recommended due to, among other reasons: cases of HCC seen in non-cirrhotic individuals; cases of progression from F3 to F4 disease in patients who had achieved SVR; and frequency of imaging studies performed in F3 patients to evaluate for progression to cirrhosis with secondary benefit of HCC screening.

Primary Care Evaluation of Chronic Hepatitis B

What populations are at higher risk of testing positive for hepatitis B?

Blood/Body Fluid Exposures
- IVDU
- Hemodialysis
- Healthcare workers
- Men who have sex with men
- Partners/family of HBV(+) person
- Infants of HBV(+) mother
- Hx of incarceration

Frequent Co-Infections
- HIV (+) individuals
- HCV (+) individuals

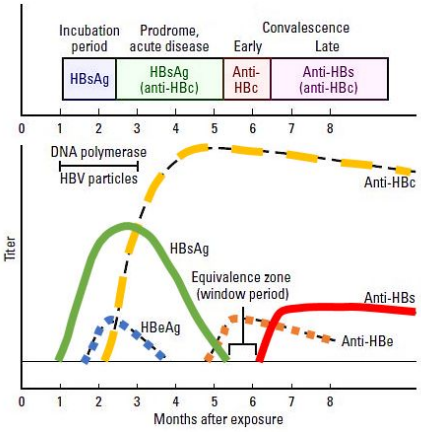
Immunosuppressed
- Chemotherapy
- Individuals on TNFa-inhibitors

Hx of chronic LFT elevation

Endemic Regions (>2% prevalence)
- China / Southeast Asia
- Africa
- South America
- Middle East
- Alaska!

How do you interpret these Hepatitis B Serologies?

HBsAg	HBsAb	HBcAb	Diagnosis
-	+	-	Immune 2/2 vaccine
-	+	+	Immune 2/2 prior infection
+	-	+	Actively infected
-	-	+	1) Remote infection 2) False (+) HBcAb 3) Low infectivity / latent chronic infection 4) Resolving acute infection



You have diagnosed a patient with chronic HBV. What additional work-up do you need to determine treatment strategy?

Evaluate degree of liver injury/cirrhosis:
- BMP, LFTs, coags
- Liver elastography

Screen for co-infections: HIV, HCV, HDV

Immunize: HAV if not immune

Evaluate for HCC: RUQ ultrasound, AFP x 6-12 months

Evaluate level of viral activity
- **HB e Antigen:** if positive, high replicative state / infectivity
- **HB e Antibody**: if positive, predictor of viral clearance
- **HBV Viral DNA**: when > 20,000, suggests high viral activity and replication

Which patients with chronic hepatitis B would you refer for treatment?

Refer patients for treatment if they have with cirrhosis, acute liver injury, or if they are pregnant

	HBeAg	HBV DNA	Liver Injury	Treatment
Immune Tolerant	+	>1 million	Normal = <2x ULN	**Close monitoring**. Consider treatment if >40yo, family hx of HCC, ≥ F2 liver fibrosis either on fibroscan or biopsy
Immune Active	+	>20,000	Elevated	**Treat**
Immune Reactivation	-	> 2,000	Elevated	**Treat**
Inactive Chronic Infection	-	< 2,000	Normal	**Close monitoring.** Treat if HBV DNA, ALT increases

What are the goals of treatment?
- Seroconversion: HBeAg (+) and HBeAb (-) → HBeAg (-) and HBeAb (+)
- Reduce HBV Viral load
- Normalize ALT

What agents are commonly used for treatment?
- **Pegylated Interferon Alpha**: ~12 months. Seroconversion achieved in 30% of patients
- **Nucleotide reverse transcriptase inhibitors**: up to 36 months. Continued until 6-12 months after seroconversion (25%)
  - Entecavir & Tenofovir are first-line
  - Adefovir, Lamivudine, Telbivudine have high rates of resistance
  - All require renal function monitoring

Primary References

Hepatitis C AASLD/IDSA Guidance

For a full listing of recommendations, along with strength of recommendation, please refer to:

AASLD/IDSA HCV Guidance Panel. Hepatitis C guidance: AASLD-IDSA recommendations for testing, managing, and treating adults infected with hepatitis C virus. Hepatology. 2015, doi:10.1002/hep.27950.

Website: http://www.hcvguidelines.org/
App: http://hcv.guidelinecentral.com/

CDC Viral Hepatitis-Hepatitis C Information

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